What is claimed is:

1. A compound according to Formula I,

or a pharmaceutically acceptable salt, hydrate, or prodrug thereof, wherein,

 $R^1$  is selected from optionally substituted  $C_{1-10}$ alkyl, optionally substituted aryl- $C_{1-10}$ alkyl, optionally substituted heterocyclyl, and optionally substituted heterocyclyl- $C_{1-10}$ alkyl;

R<sup>2</sup> is selected from -H and optionally substituted C<sub>1-6</sub>alkyl;

or R<sup>1</sup> and R<sup>2</sup> combine to form an optionally substituted three- to seven-membered heteroalicyclic;

A is a C<sub>1-3</sub>alkylene optionally substituted with one to four of R<sup>6</sup>;

B is selected from -O-,  $-N(R^4)$ -,  $-S(O)_{0.2}$ - and  $-N(CH_2)_2N(CH_2)_2-S(O)_{0.2}$ -;

X is selected from =0, =S, and  $=NR^7$ ;

Y is selected from =0, =S, and  $=NR^7$ ;

Z is C; or

Z=Y is either absent or -CH<sub>2</sub>-:

R<sup>3</sup> is selected from -H, halogen, trihalomethyl, -OR<sup>5</sup>, -N(R<sup>5</sup>)R<sup>5</sup>, -N(R<sup>5</sup>)SO<sub>2</sub>R<sup>5</sup>, -N(R<sup>5</sup>)C(O)R<sup>5</sup>, -NCO<sub>2</sub>R<sup>5</sup>, optionally substituted alkoxy, optionally substituted alkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heterocyclyl, and optionally substituted heterocyclylalkyl;

R<sup>4</sup> is selected from -H and optionally substituted C<sub>1-6</sub>alkyl; or

- R<sup>4</sup> and one of R<sup>6</sup>, together with the atoms to which they are attached, combine to form an optionally substituted five- to seven-membered non-aromatic ring;
- each R<sup>5</sup> is independently selected from -H, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclylalkyl;

1:

two of R<sup>5</sup>, together with the atom or respective atoms to which they are attached, can combine to form an optionally substituted five- to seven-membered heterocyclic;

- each R<sup>6</sup> is independently selected from -H, halogen, trihalomethyl, -CN, -NO<sub>2</sub>, -NH<sub>2</sub>, -OR<sup>5</sup>, -NR<sup>5</sup>R<sup>5</sup>, -S(O)<sub>0-2</sub>R<sup>5</sup>, -SO<sub>2</sub>NR<sup>5</sup>R<sup>5</sup>, -CO<sub>2</sub>R<sup>5</sup>, -C(O)NR<sup>5</sup>R<sup>5</sup>, -N(R<sup>5</sup>)SO<sub>2</sub>R<sup>5</sup>, -N(R<sup>5</sup>)C(O)R<sup>5</sup>, -N(R<sup>5</sup>)CO<sub>2</sub>R<sup>5</sup>, -C(O)R<sup>5</sup>, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted heterocyclyl, optionally substituted lower heterocyclylalkyl, and optionally substituted lower arylalkyl;
- two of R6, together with the atom or atoms to which they are attached, can combine to form a three to seven-membered non-aromatic ring; and
- each R<sup>7</sup> is independently selected from -H, -NO<sub>2</sub>, -NH<sub>2</sub>, -N(R<sup>5</sup>)R<sup>5</sup>, -CN, -OR<sup>5</sup>, optionally substituted lower alkyl, optionally substituted heteroalicyclylalkyl, optionally substituted aryl, optionally substituted arylalkyl and optionally substituted heteroalicyclic;
- provided the compound is not one of: 3-benzoylamino-3-phenyl-propionic acid (6-methoxy-benzothiazol-2-ylcarbamoyl)-methyl ester, N-(3,4-dichloro-benzyl)-2-[4-(4-pyridin-2-yl-pyrimidin-2-yl)-phenoxy]-acetamide, 2-(5,6-Dimethyl-4-oxo-4H-thieno[2,3-d]pyrimidin-3-yl)-N-[(6-methoxy-benzothiazol-2-ylcarbamoyl)-methyl]-acetamide, (Naphthalen-1-ylcarbamoylmethylsulfanyl)-acetic acid (5-bromo-pyridin-2-ylcarbamoyl)-methyl ester, (benzooxazol-2-ylsulfanyl)-acetic acid (5-chloro-pyridin-2-ylcarbamoyl)-methyl ester, and 4-[2-(5,6-dimethyl-4-oxo-4H-thieno[2,3-d]pyrimidin-3-yl)-acetylamino]-N-(6-methoxy-benzothiazol-2-yl)-butyramide.
- 2. The compound of claim 1, according to one of the following formulae:

$$(R^{8})_{0-6}$$
II

III

III

80

Ţ

$$(R^{8})_{0-5} = \begin{pmatrix} (R^{8})_{0-4} & & & \\ R^{6} & R^{6} & O \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & &$$

wherein R<sup>2</sup>, R<sup>3</sup>, R<sup>6</sup>, and B are as defined above; Z is a five- to seven-membered ring; each R<sup>8</sup> is independently selected from -H, halogen, trihalomethyl, -CN, -NO<sub>2</sub>, -NH<sub>2</sub>, -OR<sup>5</sup>, -NR<sup>5</sup>R<sup>5</sup>, -S(O)<sub>0-2</sub>R<sup>5</sup>, -SO<sub>2</sub>NR<sup>5</sup>R<sup>5</sup>, -CO<sub>2</sub>R<sup>5</sup>, -C(O)NR<sup>5</sup>R<sup>5</sup>, -N(R<sup>5</sup>)SO<sub>2</sub>R<sup>5</sup>, -N(R<sup>5</sup>)C(O)R<sup>5</sup>, -N(R<sup>5</sup>)CO<sub>2</sub>R<sup>5</sup>, -C(O)R<sup>5</sup>, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted heterocyclylalkyl, and optionally substituted arylalkyl; two of R<sup>8</sup>, together with the atom or atoms to which they are attached, can combine to form a three-to seven-membered ring; and E is selected from -O-, -N(R<sup>9</sup>)-, -CH<sub>2</sub>-, and -S(O)<sub>0-2</sub>-, where R<sup>9</sup> is selected from -H, trihalomethyl, -S(O)<sub>0-2</sub>R<sup>5</sup>, -SO<sub>2</sub>NR<sup>5</sup>R<sup>5</sup>, -CO<sub>2</sub>R<sup>5</sup>, -C(O)NR<sup>5</sup>R<sup>5</sup>, -C(O)R<sup>5</sup>, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted heterocyclylalkyl, and optionally substituted arylalkyl.

- 3. The compound according to claim 2, wherein B is selected from -O-,  $-N(R^4)$ -, and  $-S(O)_{0-1}$ -.
- 4. The compound according to claim 3, according to either formula II or III.
- 5. The compound according to claim 4, wherein  $R^4$  is -H or  $C_{1.6}$ alkyl.
- 6. The compound according to claim 5, wherein  $R^2$  is -H or  $C_{1-6}$ alkyl.
- 7. The compound of claim 6, according to formula **Ha**.

IIa

8. The compound according to claim 7, wherein each R<sup>6</sup> is independently selected from -H, trihalomethyl, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, and optionally substituted arylalkyl.

9. The compound according to claim 8, wherein one of R<sup>6</sup> is -H, and the other R<sup>6</sup> is selected from trihalomethyl, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, and optionally substituted arylalkyl.

- 10. The compound according to claim 9, wherein R<sup>3</sup> is selected from optionally substituted alkoxy, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclylalkyl.
- 11. The compound according to claim 10, wherein R<sup>3</sup> is selected from lower alkyl substituted with an optionally substituted aryloxy or an optionally substituted heteroaryloxy, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heteroaryl, and optionally substituted lower heteroarylalkyl.
- 12. The compound according to claim 11, wherein R<sup>3</sup> is an aryl, said aryl substituted with at least one of an optionally substituted aryl and an optionally substituted heteroaryl.
- 13. The compound according to claim 12, wherein R<sup>3</sup> is an optionally substituted bisphenyl.
- 14. The compound according to claim 13, wherein R3 comprises an optionally substituted phenylene, wherein the point of attachment of R3 according to formula IIa, and an optionally substituted phenyl bear a para relationship to one another about said optionally substituted phenylene.
- 15. A compound for modulating at least one kinase activity according to formula VI,

VI

or a pharmaceutically acceptable salt, hydrate, or prodrug thereof, wherein, each of  $R^{11}$  and  $R^{12}$  is independently selected from -H, halogen, trihalomethyl, -CN, -NO<sub>2</sub>, -NR<sup>14</sup>R<sup>14</sup>, -S(O)<sub>0-2</sub>R<sup>14</sup>, -SO<sub>2</sub>NR<sup>14</sup>R<sup>14</sup>, -CO<sub>2</sub>R<sup>14</sup>, -C(O)NR<sup>14</sup>R<sup>14</sup>, -N(R<sup>14</sup>)SO<sub>2</sub>R<sup>14</sup>, -N(R<sup>14</sup>)C(O)R<sup>14</sup>, -N(R<sup>14</sup>)CO<sub>2</sub>R<sup>14</sup>, -OR<sup>14</sup>, -C(O)R<sup>14</sup>, optionally substituted lower alkyl, optionally substituted alkoxy, optionally substituted aryl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, and optionally substituted arylalkyl;

R<sup>14</sup> is selected from -H, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclylalkyl;

each of X and Y is independently selected from -O-,  $-N(R^{14})$ -, and  $-S(O)_{0-2}$ -;

n is selected from an integer from 0-2;

Ar is an optionally substituted aryl that may be substituted with up to three R<sup>11</sup>, wherein two adjacent R<sup>11</sup>'s, together with the annular atoms to which they are attached, can form a five- to seven-membered ring containing up to three heteroatoms and optionally substituted with up to three of R<sup>15</sup>;

each  $R^{15}$  is independently selected from -H, halo, trihalomethyl, -CN, -NO<sub>2</sub>, -OR<sup>16</sup>, -N(R<sup>16</sup>)R<sup>16</sup>, -S(O)<sub>0-2</sub>R<sup>16</sup>, -SO<sub>2</sub>N(R<sup>16</sup>)R<sup>16</sup>, -CO<sub>2</sub>R<sup>16</sup>, -C(=O)N(R<sup>16</sup>)R<sup>16</sup>, -C(=NR<sup>17</sup>)N(R<sup>16</sup>)R<sup>16</sup>, -C(=NR<sup>17</sup>)R<sup>16</sup>, -N(R<sup>16</sup>)SO<sub>2</sub>R<sup>16</sup>, -N(R<sup>16</sup>)C(O)R<sup>16</sup>, -NCO<sub>2</sub>R<sup>16</sup>, -C(=O)R<sup>16</sup>, optionally substituted alkoxy, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower heterocyclylalkyl;

R<sup>16</sup> is selected from -H, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclylalkyl; and

R<sup>17</sup> is selected from -H, -CN, -NO<sub>2</sub>, -OR<sup>16</sup>, -S(O)<sub>0-2</sub>R<sup>16</sup>, -CO<sub>2</sub>R<sup>16</sup>, optionally substituted lower alkyl, optionally substituted lower alkynyl.

- 16. A compound according to claim 15, wherein X is O.
- 17. A compound according to claim 16, wherein Y is O.
- 18. A compound according to claim 17, wherein R<sup>11</sup> is -H.
- 19. A compound according to claim 18, wherein R<sup>12</sup> is -H.
- 20. A compound according to claim 19, wherein n is 1.
- 21. A compound according to claim 20, wherein Ar is substituted aryl and two adjacent R<sup>11</sup>'s, together with the annular atoms to which they are attached, form a substituted six-membered ring containing up to three heteroatoms.

22. A compound according to claim 20, wherein Ar is substituted aryl and two adjacent R<sup>11</sup>'s, together with the annular atoms to which they are attached, form a substituted seven-membered ring containing up to three heteroatoms.

23. The compound according to claim 1 or 15, selected from the following:

Table 3

| Entry | Name   | Structure          |
|-------|--|--------------------|
| 1     | N-{2-oxo-2-(1,2,3,4-<br>tetrahydronaphthalen-1-<br>ylamino)ethyl]-4-<br>(pentyloxy)benzamide                 | HN CH3             |
| 2     | N~2~-[({4-<br>[(phenylmethyl)oxy]phenyl}oxy)acet<br>yl]-N-(1,2,3,4-tetrahydronaphthalen-<br>1-yl)glycinamide |                    |
| 3     | N~2~-{[(4-bromophenyl)oxy]acetyl}-<br>N-(1,2,3,4-tetrahydronaphthalen-1-<br>yl)glycinamide                   | PH H-COBR          |
| 4     | 4'-ethyl-N-[2-oxo-2-(1,2,3,4-<br>tetrahydronaphthalen-1-<br>ylamino)ethyl]biphenyl-4-<br>carboxamide         | HN CH <sub>3</sub> |

Table 3

| Entry | Name  | Structure                        |
|-------|---|----------------------------------|
| 5     | 4'-ethyl-N-[1-methyl-2-oxo-2-<br>(1,2,3,4-tetrahydronaphthalen-2-<br>ylamino)ethyl]biphenyl-4-<br>carboxamide | H <sub>3</sub> C CH <sub>3</sub> |
| 6     | 4-(hexyloxy)-N-[2-oxo-2-(1,2,3,4-<br>tetrahydronaphthalen-1-<br>ylamino)ethyl]benzamide                       | HN CH <sub>3</sub>               |
| 7     | 2-cyclopentyl-N-[2-oxo-1-pyridin-3-yl-2-(1,2,3,4-tetrahydronaphthalen-1-ylamino)ethyl]-2-phenylacetamide      |                                  |
| 8     | 4-(heptyloxy)-N-[2-oxo-2-(1,2,3,4-<br>tetrahydronaphthalen-1-<br>ylamino)ethyl]benzamide                      | HN CH <sub>3</sub>               |
| 9     | N-[1-methyl-2-oxo-2-(1,2,3,4-<br>tetrahydronaphthalen-2-<br>ylamino)ethyl]-4-<br>(pentyloxy)benzamide         | H,c H, CH,                       |

Table 3

| [     | <u> </u>   |  |
|-------|--|--|
| Entry | Name   | Structure  |
| 10    | 4-hexyl-N-[2-oxo-2-(1,2,3,4-<br>tetrahydronaphthalen-1-<br>ylamino)ethyl]benzamide                                   | HN CH <sub>3</sub>                                   |
| 11    | N-[2-oxo-2-(1,2,3,4-<br>tetrahydronaphthalen-1-<br>ylamino)ethyl]-4-pentylbenzamide                                  | HN CH <sub>3</sub>                                   |
| 12    | 4-heptyl-N-[2-oxo-2-(1,2,3,4-<br>tetrahydronaphthalen-1-<br>ylamino)ethyl]benzamide                                  | HN CH <sub>3</sub>                                   |
| 13    | Nalpha-{[5,6-bis(methyloxy)-1H-<br>indol-2-yl]carbonyl}-N-(1,2,3,4-<br>tetrahydronaphthalen-1-<br>yl)tryptophanamide | HN O CH <sub>3</sub> CH <sub>3</sub> CH <sub>3</sub> |

Table 3

| Entry | Name   | Structure  |
|-------|--|--|
| 14    | Nalpha-{[4-<br>(butyloxy)phenyl]carbonyl}-N-<br>(1,2,3,4-tetrahydronaphthalen-1-<br>yl)tryptophanamide   | H <sub>3</sub> C O                                   |
| 15    | 5-{(2E)-3-[3,4-<br>bis(methyloxy)phenyl]prop-2-enoyl}-<br>N-[2-(3-chlorophenyl)ethyl]-4,5,6,7-<br>tetrahydro-3H-imidazo[4,5-<br>c]pyridine-6-carboxamide | Q-OCH <sub>3</sub>                                   |
| 16    | N-[2-oxo-1-pyridin-3-yl-2-(1,2,3,4-<br>tetrahydronaphthalen-1-<br>ylamino)ethyl]-4-(1H-1,2,4-triazol-1-<br>yl)benzamide                                  |  |
| 17    | Nalpha-{(2E)-3-[3,4-<br>bis(methyloxy)phenyl]prop-2-enoyl}-<br>N-(1,2,3,4-tetrahydronaphthalen-1-<br>yl)tryptophanamide                                  | H <sub>3</sub> C.OL<br>CH <sub>3</sub> HN<br>HN<br>N |

Table 3

| Entry | Name  | Structure                                 |
|-------|---|---|
| 18    | 4-(butyloxy)-N-[1-methyl-2-oxo-2-<br>(1,2,3,4-tetrahydronaphthalen-2-<br>ylamino)ethyl]benzamide                  | N H<br>H <sub>3</sub> C O CH <sub>3</sub> |
| 19    | N-[1-methyl-2-oxo-2-(1,2,3,4-<br>tetrahydronaphthalen-2-<br>ylamino)ethyl]-4-<br>[(phenylmethyl)oxy]benzamide     | H <sub>3</sub> C H                        |
| 20    | 3,5-dimethyl-N-[2-oxo-2-(1,2,3,4-<br>tetrahydronaphthalen-1-<br>ylamino)ethyl]-4-<br>[(phenylmethyl)oxy]benzamide | HN CH <sub>3</sub>                        |
| 21    | N~2~-({[4-<br>(butyloxy)phenyl]amino}carbonyl)-<br>N-(2-phenylethyl)-O-<br>(phenylmethyl)serinamide               | NH CH <sub>3</sub>                        |

Table 3

| Entry | Name   | Structure                       |
|-------|--|---------------------------------|
| . 22  | (2S)-N~1~-(4-butylphenyl)-N~2~- [(3,4- dichlorophenyl)methyl]pyrrolidine- 1,2-dicarboxamide  | CI H H N O HN O CH <sub>3</sub> |
| 23    | N-[6-(methyloxy)-1,3-benzothiazol-<br>2-yl]-4-{[(4-oxo-5,6,7,8-<br>tetrahydro[1]benzothieno[2,3-<br>d]pyrimidin-3(4H)-<br>yl)acetyl]amino}butanamide | O NH S O CH <sub>3</sub>        |
| 24    | (2S)-N~2~-[(3,4-<br>dichlorophenyl)methyl]-N~1~-[4-(1-<br>methylethyl)phenyl]pyrrolidine-1,2-<br>dicarboxamide                                       | CI HH H N O HN CH3              |
| 25    | N~2~-{[(4-bromophenyl)oxy]acetyl}-<br>N-[(3,4-<br>dichlorophenyl)methyl]glycinamide  | Br<br>ONH<br>HNO<br>O           |

(: •

Table 3

| Entry | Name   | Structure                                |
|-------|--|--|
| 26    | N-[2-oxo-1-pyridin-3-yl-2-(1,2,3,4-<br>tetrahydronaphthalen-1-<br>ylamino)ethyl]-4-[(E)-<br>phenyldiazenyl]benzamide | H-O-H-O-N-O-N-O-N-O-N-O-N-O-N-O-N-O-N-O- |
| 27    | 4-(butyloxy)-N-[2-oxo-2-(1,2,3,4-<br>tetrahydronaphthalen-1-<br>ylamino)ethyl]benzamide                              | HN CH <sub>3</sub>                       |
| 28    | N~2~-({[3-<br>(methyloxy)phenyl]oxy}acetyl)-N-<br>(1,2,3,4-tetrahydronaphthalen-1-<br>yl)glycinamide                 | H <sub>3</sub> C <sub>0</sub>            |
| 29    | 4-butyl-N-[2-oxo-2-(1,2,3,4-<br>tetrahydronaphthalen-1-<br>ylamino)ethyl]benzamide                                   | HN CH,                                   |
| 30    | N~2~-{(2E)-3-[3,4-<br>bis(methyloxy)phenyl]prop-2-enoyl}-<br>N-(diphenylmethyl)-O-<br>(phenylmethyl)serinamide       | H <sub>3</sub> °C. O CH <sub>3</sub>     |

Table 3

| Entry | Name  | Structure   |
|-------|---|---|
| 31    | N-(1,2,3,4-tetrahydronaphthalen-1-<br>yl)-N~2~-[({4-<br>[(trifluoromethyl)oxy]phenyl}oxy)ace<br>tyl]glycinamide | N N N F F F   |
| 32    | N-{3-methyl-1-[(1,2,3,4-<br>tetrahydronaphthalen-1-<br>ylamino)carbonyl]butyl}biphenyl-4-<br>carboxamide        | NH<br>OH<br>H <sub>3</sub> C                                      |
| 33    | N~2~-({[4-(1,1-dimethylethyl)phenyl]oxy}acetyl)-N-(1,2,3,4-tetrahydronaphthalen-1-yl)glycinamide                | N-CH <sub>3</sub> CH <sub>3</sub> CH <sub>3</sub> CH <sub>3</sub> |
| 34    | N~2~-{[(4-chlorophenyl)oxy]acetyl}-<br>N-(1,2,3,4-tetrahydronaphthalen-1-<br>yl)glycinamide                     |   |
| 35    | N~2~-{[4-<br>(pentyloxy)phenyl]carbonyl}-N-<br>(1,2,3,4-tetrahydronaphthalen-1-<br>yl)leucinamide               | NH<br>O=NH<br>H <sub>3</sub> C<br>H <sub>3</sub> C                |

Table 3

| <b>5</b> |  | C   |
|----------|--|---|
| Entry    | Name   | Structure   |
| 36       | 4-(hexyloxy)-N-[1-methyl-2-oxo-2-<br>(1,2,3,4-tetrahydronaphthalen-2-<br>ylamino)ethyl]benzamide   | H <sub>3</sub> C H<br>H <sub>3</sub> C OH <sub>3</sub>                |
| 37       | 2-{[6-(methyloxy)-1,3-benzothiazol-<br>2-yl]amino}-2-oxoethyl 3-phenyl-3-<br>[(phenylcarbonyl)amino]propanoate                               | H <sub>3</sub> C <sub>1</sub> O-O-N O O O O O O O O O O O O O O O O O |
| 38       | N-[(3,4-dichlorophenyl)methyl]-2-<br>{[4-(4-pyridin-2-ylpyrimidin-2-<br>yl)phenyl]oxy}acetamide  | O ZH  |
| 39       | N-(2,3-dihydro-1,4-benzodioxin-2-<br>ylmethyl)-3-[3-(ethyloxy)propyl]-4-<br>oxo-2-thioxo-1,2,3,4-<br>tetrahydroquinazoline-7-<br>carboxamide |   |

Table 3

| Entry | Name  | Structure   |
|-------|---|---|
| 40    | N~2~-[(5,6-dimethyl-4-<br>oxothieno[2,3-d]pyrimidin-3(4H)-<br>yl)acetyl]-N-[6-(methyloxy)-1,3-<br>benzothiazol-2-yl]glycinamide | CH <sub>3</sub> |
| 41    | 2-{4-[(2-naphthalen-1-<br>ylethyl)sulfonyl]piperazin-1-yl}-N-<br>pyridin-2-ylacetamide  | ON NH Z   |
| 42    | N-(2,3-dihydro-1,4-benzodioxin-2-<br>ylmethyl)-11-oxo-10,11-dihydro-5H-<br>dibenzo[b,e][1,4]diazepine-8-<br>carboxamide         |   |
| 43    | N-[2-oxo-2-(1,2,3,4-<br>tetrahydronaphthalen-1-<br>ylamino)ethyl]biphenyl-4-<br>carboxamide                                     | H Z Z   |

( **.**..

Table 3

| Entry | Name  | Structure                                |
|-------|---|--|
| 44    | N-[2-oxo-2-(1,2,3,4-<br>tetrahydronaphthalen-1-<br>ylamino)ethyl]naphthalene-2-<br>carboxamide                          | HN HN H                                  |
| 45    | N-[2-oxo-2-(1,2,3,4-<br>tetrahydronaphthalen-1-<br>ylamino)ethyl]-4-<br>[(trifluoromethyl)oxy]benzamide                 |  |
| 46    | N-[2-oxo-2-(1,2,3,4-<br>tetrahydronaphthalen-1-<br>ylamino)ethyl]quinoline-3-<br>carboxamide                            | HN                                       |
| 47    | N~2~-({[3,5-<br>bis(trifluoromethyl)phenyl]amino}car<br>bonyl)-N-(1,2,3,4-<br>tetrahydronaphthalen-1-<br>yl)glycinamide | NH H H F F F F F F F F F F F F F F F F F |

Table 3

| Entry | Name   | Structure          |
|-------|--|--------------------|
| 48    | N~2~-{[(3-<br>ethylphenyl)amino]carbonyl}-N-<br>(1,2,3,4-tetrahydronaphthalen-1-<br>yl)glycinamide   | ON CH <sub>3</sub> |
| 49    | N-[2-oxo-2-(1,2,3,4-<br>tetrahydronaphthalen-1-<br>ylamino)ethyl]-4-<br>(phenyloxy)benzamide         | HN N               |
| 50    | 4-cyclohexyl-N-[2-oxo-2-(1,2,3,4-<br>tetrahydronaphthalen-1-<br>ylamino)ethyl]benzamide              | HZ H               |
| 51    | N-[2-oxo-2-(1,2,3,4-<br>tetrahydronaphthalen-1-<br>ylamino)ethyl]-4-<br>[(phenylmethyl)oxy]benzamide |                    |
| 52    | 4'-ethyl-N-{2-oxo-2-<br>[(phenylmethyl)amino]ethyl}bipheny<br>I-4-carboxamide                        | CH <sub>3</sub>    |

Table 3

| Entry | Name   | Structure          |
|-------|--|--------------------|
| 53    | N-[2-(cyclohexylamino)-2-oxoethyl]-<br>4'-ethylbiphenyl-4-carboxamide  | HN CH <sub>3</sub> |
| 54    | N-(2-{[(3,4-<br>dichlorophenyl)methyl]amino}-2-<br>oxoethyl)-4'-ethylbiphenyl-4-<br>carboxamide                                | CH <sup>3</sup>    |
| . 55  | N~2~-<br>[{[cyclopentyl(phenyl)acetyl]amino}(<br>pyridin-3-yl)acetyl]-N-(1,2,3,4-<br>tetrahydronaphthalen-1-<br>yl)glycinamide |                    |
| 56    | 4-hydroxy-N-[2-oxo-2-(1,2,3,4-<br>tetrahydronaphthalen-1-<br>ylamino)ethyl]benzamide   |                    |

Table 3

| Entry | Name   | Structure   |
|-------|--|---|
| 57    | N-[2-(1,3-dihydro-2H-isoindol-2-yl)-<br>2-oxoethyl]-4'-ethylbiphenyl-4-<br>carboxamide                           | N N N   |
| 58    | 4-morpholin-4-yl-N-[2-oxo-2-<br>(1,2,3,4-tetrahydronaphthalen-1-<br>ylamino)ethyl]benzamide                      |   |
| 59    | 5,6-bis(methyloxy)-N-[2-oxo-2-<br>(1,2,3,4-tetrahydronaphthalen-1-<br>ylamino)ethyl]-1H-indole-2-<br>carboxamide | O-CH <sub>3</sub> O-CH <sub>3</sub> O-CH <sub>3</sub> |
| 60    | N-[2-(3,4-dihydroisoquinolin-2(1H)-<br>yl)-2-oxoethyl]-4'-ethylbiphenyl-4-<br>carboxamide                        | CH <sub>3</sub>                                       |
| 61    | 4'-ethyl-N-{2-oxo-2-[(1S)-1,2,3,4-<br>tetrahydronaphthalen-1-<br>ylamino]ethyl}biphenyl-4-<br>carboxamide        | HIN CH <sub>3</sub>                                   |

Table 3

| Entry | Name   | Structure   |
|-------|--|---|
| 62    | 2-amino-N~4~-(2,3-dihydro-1,4-<br>benzodioxin-2-ylmethyl)-N~1~-[3-<br>(ethyloxy)propyl]benzene-1,4-<br>dicarboxamide | NH <sub>2</sub>   |
| 63    | N-{3-[(2-{[6-(methyloxy)-1,3-<br>benzothiazol-2-yl]amino}-2-<br>oxoethyl)amino]-3-oxo-1-<br>phenylpropyl}benzamide   | H <sub>3</sub> C <sub>0</sub> H <sub>0</sub> O H <sub>0</sub> O     |
| 64    | 4'-ethyl-N-(2-{[6-(methyloxy)-1,3-<br>benzothiazol-2-yl]amino}-2-<br>oxoethyl)biphenyl-4-carboxamide                 | H <sub>3</sub> C <sub>O</sub> N N N N N N N N N N N N N N N N N N N |
| 65    | N-{2-[(2,3-dihydro-1,4-benzodioxin-<br>2-ylmethyl)amino]-2-oxoethyl}-4'-<br>ethylbiphenyl-4-carboxamide              | CH <sub>3</sub>   |
| 66    | 4'-ethyl-N-methyl-N-[2-oxo-2-<br>(1,2,3,4-tetrahydronaphthalen-1-<br>ylamino)ethyl]biphenyl-4-<br>carboxamide        | CH <sub>3</sub> CH <sub>3</sub>                                     |

Table 3

| Entry | Name  | Structure                              |
|-------|---|--|
| 67    | 4'-ethyl-N-[2-(naphthalen-1-<br>ylamino)-2-oxoethyl]biphenyl-4-<br>carboxamide                  | HN CH <sub>3</sub>                     |
| 68    | 4'-ethyl-N-[2-oxo-2-(4-<br>phenylpiperazin-1-yl)ethyl]biphenyl-<br>4-carboxamide                | CH <sub>3</sub>                        |
| 69    | N~2~-(biphenyl-4-ylmethyl)-N-<br>(1,2,3,4-tetrahydronaphthalen-1-<br>yl)glycinamide             |  |
| 70    | 4-(1H-imidazol-1-yl)-N-[2-oxo-2-<br>(1,2,3,4-tetrahydronaphthalen-1-<br>ylamino)ethyl]benzamide | HN N N N N N N N N N N N N N N N N N N |
| 71    | 4-(1,3-oxazol-5-yl)-N-[2-oxo-2-<br>(1,2,3,4-tetrahydronaphthalen-1-<br>ylamino)ethyl]benzamide  | HN HN ON                               |

Table 3

| Entry | Name  | Structure          |
|-------|---|--------------------|
| 72    | N~2~-{[(2-biphenyl-4-<br>ylethyl)amino]carbonyl}-N-(1,2,3,4-<br>tetrahydronaphthalen-1-<br>yl)glycinamide |                    |
| 73    | N~2~-[(biphenyl-4-<br>ylamino)carbonyl]-N-(1,2,3,4-<br>tetrahydronaphthalen-1-<br>yl)glycinamide          |                    |
| 74    | 4'-ethyl-N-(2-{[(2-<br>methylphenyl)methyl]amino}-2-<br>oxoethyl)biphenyl-4-carboxamide                   | CH <sub>3</sub>    |
| 75    | 4'-ethyl-N-{2-oxo-2-[(2-<br>phenylethyl)amino]ethyl}biphenyl-4-<br>carboxamide                            | CH <sub>3</sub>    |
| 76    | 4'-ethyl-N-{2-oxo-2-[(1R)-1,2,3,4-<br>tetrahydronaphthalen-1-<br>ylamino]ethyl}biphenyl-4-<br>carboxamide | HN CH <sub>3</sub> |

Table 3

| Entry | Name   | Structure                              |
|-------|--|--|
| 77    | N-[2-oxo-2-(1,2,3,4-<br>tetrahydronaphthalen-1-<br>ylamino)ethyl]-4-piperidin-1-<br>ylbenzamide                | HN N N N N N N N N N N N N N N N N N N |
| 78    | 4'-ethyl-N-{2-oxo-2-[(1-<br>phenylethyl)amino]ethyl}biphenyl-4-<br>carboxamide                                 | HN CH <sub>3</sub>                     |
| 79    | 4'-ethyl-N-[2-oxo-2-({[2-<br>(trifluoromethyl)phenyl]methyl}amin<br>o)ethyl]biphenyl-4-carboxamide             | HN CH <sub>3</sub>                     |
| 80    | N-[2-oxo-2-(1,2,3,4-<br>tetrahydronaphthalen-1-<br>ylamino)ethyl]quinoline-6-<br>carboxamide                   | HN NH                                  |
| 81    | N-(3-oxo-3-{[2-oxo-2-(1,2,3,4-<br>tetrahydronaphthalen-1-<br>ylamino)ethyl]amino}-1-<br>phenylpropyl)benzamide |  |

Table 3

| Entry | Name  | Structure                                     |
|-------|---|---|
| 82    | N-[2-oxo-2-(1,2,3,4-<br>tetrahydronaphthalen-1-<br>ylamino)ethyl]-5,6,7,8-<br>tetrahydronaphthalene-2-<br>carboxamide |   |
| 83    | 4'-ethyl-N-{2-oxo-2-[(1-<br>phenylpropyl)amino]ethyl}biphenyl-<br>4-carboxamide                                       | HN CH <sub>3</sub>                            |
| 84    | 3-(acetylamino)-N-(2-{[6-<br>(methyloxy)-1,3-benzothiazol-2-<br>yl]amino}-2-oxoethyl)-3-<br>phenylpropanamide         | H <sub>3</sub> C <sub>0</sub> CH <sub>3</sub> |
| 85    | N-(phenylcarbonyl)-beta-alanyl-N-<br>[6-(methyloxy)-1,3-benzothiazol-2-<br>yl]glycinamide                             | H <sub>3</sub> C <sub>1</sub> O S H H O       |
| 86    | N-[2-oxo-2-(5,6,7,8-<br>tetrahydronaphthalen-1-<br>ylamino)ethyl]quinoline-6-<br>carboxamide                          |   |

Table 3

| Entry | Name   | Structure |
|-------|--|-----------|
| 87    | N-[2-oxo-2-(5,6,7,8-<br>tetrahydronaphthalen-1-<br>ylamino)ethyl]quinoline-3-<br>carboxamide           | HN NH     |
| 88    | N-[2-oxo-2-(1,2,3,4-<br>tetrahydronaphthalen-1-<br>ylamino)ethyl]-3-piperidin-1-<br>ylpropanamide      | HN N N    |
| 89    | N-[2-oxo-2-(5,6,7,8-<br>tetrahydronaphthalen-1-<br>ylamino)ethyl]-4-piperidin-1-<br>ylbenzamide        | HN HN H   |
| 90    | N-(3-{[2-(1,3-benzothiazol-2-<br>ylamino)-2-oxoethyl]amino}-3-oxo-<br>1-phenylpropyl)benzamide         |           |
| 91    | N-[2-oxo-2-(1,2,3,4-<br>tetrahydronaphthalen-1-<br>ylamino)ethyl]-4-phenylpiperazine-<br>1-carboxamide |           |

Table 3

| Entry | Name   | Structure  |
|-------|--|--|
| 92    | N-(3-oxo-3-{[2-oxo-2-(1,3-thiazol-2-<br>ylamino)ethyl]amino}-1-<br>phenylpropyl)benzamide  |  |
| 93    | N-[3-({2-[(4-methyl-1,3-thiazol-2-<br>yl)amino]-2-oxoethyl}amino)-3-oxo-<br>1-phenylpropyl]benzamide                             | H <sub>3</sub> C N N N N N N N N N N N N N N N N N N N                                 |
| 94    | N-{3-[(2-{[5-<br>(methyloxy)[1,3]thiazolo[5,4-<br>b]pyridin-2-yl]amino}-2-<br>oxoethyl)amino]-3-oxo-1-<br>phenylpropyl}benzamide | H <sub>3</sub> C <sub>O</sub> N N N N N N N N N N N N N N N N N N N                    |
| 95    | 1,1-dimethylethyl 4-({N-[(4'-<br>ethylbiphenyl-4-<br>yl)carbonyl]glycyl}amino)-3,4-<br>dihydroisoquinoline-2(1H)-<br>carboxylate | HN CH <sub>3</sub> HN CH <sub>3</sub> H <sub>3</sub> C CH <sub>3</sub> CH <sub>3</sub> |

Table 3

| Entry | Name   | Structure                                |
|-------|--|--|
| 96    | 4'-ethyl-N-[2-oxo-2-(1,2,3,4-<br>tetrahydroisoquinolin-4-<br>ylamino)ethyl]biphenyl-4-<br>carboxamide          | HN CH <sub>3</sub>                       |
| 97    | N-{3-[(6-hydroxy-1,3-benzothiazol-<br>2-yl)amino]-3-oxo-1-<br>phenylpropyl}benzamide                           | HO S H                                   |
| 98    | N-{3-({2-[(6-hydroxy-1,3-<br>benzothiazol-2-yl)amino]-2-<br>oxoethyl}amino)-3-oxo-1-<br>phenylpropyl]benzamide | HO T'S H H O H                           |
| 99    | 2-[(5-bromopyridin-2-yl)amino]-2-<br>oxoethyl {[2-(naphthalen-1-<br>ylamino)-2-oxoethyl]thio}acetate           | HE S O O O O O O O O O O O O O O O O O O |
| 100   | 2-[(5-chloropyridin-2-yl)amino]-2-<br>oxoethyl (1,3-benzoxazol-2-<br>ylthio)acetate                            | CI S N                                   |

Table 3

| Entry | Name   | Structure             |
|-------|--|-----------------------|
| 101   | 4-{[(5,6-dimethyl-4-oxothieno[2,3-d]pyrimidin-3(4H)-yl)acetyl]amino}-<br>N-[6-(methyloxy)-1,3-benzothiazol-<br>2-yl]butanamide | H <sub>3</sub> C S NH |

- 24. A pharmaceutical composition comprising a compound according to any one of claims 1-23 and a pharmaceutically acceptable carrier.
- 25. A metabolite of the compound or the pharmaceutical composition according to any one of claims 1-24.
- A method of modulating the in vivo activity of a kinase, the method comprising 26. administering to a subject an effective amount of either the compound or the pharmaceutical composition according to any of claims 1-24, or a compound, or pharmaceutical composition comprising said compound and a pharmaceutically acceptable carrier, selected from the group consisting of 3-benzoylamino-3-phenyl-propionic acid (6-N-(3,4-dichloro-benzyl)-2-[4-(4methoxy-benzothiazol-2-ylcarbamoyl)-methyl ester, pyridin-2-yl-pyrimidin-2-yl)-phenoxy]-acetamide, 2-(5,6-dimethyl-4-oxo-4H-thieno[2,3d]pyrimidin-3-yl)-N-[(6-methoxy-benzothiazol-2-ylcarbamoyl)-methyl]-acetamide, (naphthalen-1-ylcarbamoylmethylsulfanyl)-acetic acid (5-bromo-pyridin-2-ylcarbamoyl)methyl ester, (benzooxazol-2-ylsulfanyl)-acetic acid (5-chloro-pyridin-2-ylcarbamoyl)and 4-[2-(5,6-dimethyl-4-oxo-4H-thieno[2,3-d]pyrimidin-3-yl)methyl ester, acetylamino]-N-(6-methoxy-benzothiazol-2-yl)-butyramide.
- 27. The method according to claim 26, wherein the kinase is at least one of KIAA1361, TAO, and JIK.
- 28. The method according to claim 27, wherein modulating the *in vivo* activity of the kinase comprises inhibition of said kinase.

29. A method of treating diseases or disorders associated with uncontrolled, abnormal, and/or unwanted cellular activities, the method comprising administering, to a mammal in need thereof, a therapeutically effective amount of either the compound or the pharmaceutical composition as described in any one of claims 1-24, or a compound, or pharmaceutical composition comprising said compound and a pharmaceutically acceptable carrier, selected from the group consisting of 3-benzoylamino-3-phenyl-propionic acid (6methoxy-benzothiazol-2-ylcarbamoyl)-methyl ester, N-(3,4-dichloro-benzyl)-2-[4-(4pyridin-2-yl-pyrimidin-2-yl)-phenoxy]-acetamide, 2-(5,6-Dimethyl-4-oxo-4H-thieno[2,3d]pyrimidin-3-yl)-N-[(6-methoxy-benzothiazol-2-ylcarbamoyl)-methyl]-acetamide, (Naphthalen-1-ylcarbamoylmethylsulfanyl)-acetic acid (5-bromo-pyridin-2-ylcarbamoyl)methyl ester, (benzooxazol-2-ylsulfanyl)-acetic acid (5-chloro-pyridin-2-ylcarbamoyl)-4-[2-(5,6-dimethyl-4-oxo-4H-thieno[2,3-d]pyrimidin-3-yl)methyl ester, and acetylamino]-N-(6-methoxy-benzothiazol-2-yl)-butyramide.

- 30. A method of screening for a modulator of a kinase, said kinase selected from KIAA1361, TAO, and JIK, the method comprising combining either a compound according to any one of claims 1-23, or a compound selected from the group consisting of 3-benzoylamino-3-phenyl-propionic acid (6-methoxy-benzothiazol-2-ylcarbamoyl)-N-(3,4-dichloro-benzyl)-2-[4-(4-pyridin-2-yl-pyrimidin-2-yl)-phenoxy]methyl ester, 2-(5,6-dimethyl-4-oxo-4H-thieno[2,3-d]pyrimidin-3-yl)-N-[(6-methoxyacetamide, benzothiazol-2-ylcarbamoyl)-methyl]-acetamide, (naphthalen-1ylcarbamoylmethylsulfanyl)-acetic acid (5-bromo-pyridin-2-ylcarbamoyl)-methyl ester, (benzooxazol-2-ylsulfanyl)-acetic acid (5-chloro-pyridin-2-ylcarbamoyl)-methyl ester, and 4-[2-(5,6-dimethyl-4-oxo-4H-thieno[2,3-d]pyrimidin-3-yl)-acetylamino]-N-(6-methoxybenzothiazol-2-yl)-butyramide, and at least one candidate agent and determining the effect of the candidate agent on the activity of said kinase.
- 31. A method of inhibiting proliferative activity in a cell, the method comprising administering an effective amount of a composition comprising a compound according any one of claims 1-23, or a compound selected from the group consisting of 3-benzoylamino-3-phenyl-propionic acid (6-methoxy-benzothiazol-2-ylcarbamoyl)-methyl ester, N-(3,4-dichloro-benzyl)-2-[4-(4-pyridin-2-yl-pyrimidin-2-yl)-phenoxy]-acetamide, 2-(5,6-dimethyl-4-oxo-4H-thieno[2,3-d]pyrimidin-3-yl)-N-[(6-methoxy-benzothiazol-2-ylcarbamoyl)-methyl]-acetamide, (naphthalen-1-ylcarbamoylmethylsulfanyl)-acetic acid (5-bromo-pyridin-2-ylcarbamoyl)-methyl ester, (benzooxazol-2-ylsulfanyl)-acetic acid (5-

chloro-pyridin-2-ylcarbamoyl)-methyl ester, and 4-[2-(5,6-dimethyl-4-oxo-4H-thieno[2,3-d]pyrimidin-3-yl)-acetylamino]-N-(6-methoxy-benzothiazol-2-yl)-butyramide, to a cell or a plurality of cells.